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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,775	07/19/2001	Susan Schiavi	GZ 2065.23	2672

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EXAMINER
GIBBS, TERRA C

ART UNIT	PAPER NUMBER
1635	18

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/909,775	Applicant(s) SCHIAVI ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-4,6-14 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10 & 17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to the Election filed 1/27/03, in Paper No. 16.

New claims 15-20 are acknowledged. Claims 1-20 are pending in the instant application.

Claims 1-4 and 6-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16.

Newly submitted claims 16-20 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicant's Election filed 1/27/03, in Paper No. 16, is directed to a method of reducing phosphate re-absorption by administering the FRP-4 protein. New claims 16-20 are directed to a method of reducing phosphate re-absorption by administering a polynucleotide that encodes the FRP-4 protein. New claims 16-20 are related to Group IV of the previous Office Action mailed 10/1/02 in Paper No. 14, and will be grouped and classified accordingly.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 16-20 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 5 and 15 have been examined as to the extent they read on the elected subject matter.

Election/Restrictions

Applicant's election with traverse of Group III (claim 5) in Paper No. 16 is acknowledged. The traversal is on the ground(s) that claims 1-5 are related to the single concept of regulating FRP-4 protein. Also, Applicant argues that a search of literature relating to FRP-4 protein would clearly reveal art relating to claims 1 to 5, and therefore would not place an undue burden on the Examiner. Further, Applicant argues that the methods of claims 1 to 5 in each of the Groups I, II and III are related in function, since they all relate to modulating phosphate absorption and re-absorption. Also, Applicant argues that the methods of claims 1 to 5 in each of the Groups I, II and III exhibit a disclosed relationship. Applicant also argues Groups I, II and III are classified in the same class and cannot be held to be patentably distinct. This is found persuasive (in part).

Examiner agrees that the methods of claims 1 to 4 are related in function and exhibit a disclosed relationship. Therefore Groups I and II from the previous Office Action mailed 10/1/02 in Paper No. 14, will be combined.

The new groups for the Restriction under 35 U.S.C. 121 are as followed :

I. Claims 1-4, drawn to a method of modulating phosphate homeostasis in a subject comprising altering the activity of a polypeptide encoded by FRP-4, classifiable in class 514, subclass 1.

II. Claim 5, drawn to a method of reducing phosphate re-absorption in a subject comprising delivering a FRP-4 protein, classifiable in class 514, subclass 2.

III. Claim 6, drawn to a method of reducing phosphate re-absorption in a subject comprising delivering a polynucleotide encoding a FRP-4 protein, classifiable in class 514, subclass 44.

IV. Claims 7-14, drawn to methods of screening for candidate therapeutic agents that modulate the expression and biological activity of FRP-4, classifiable in 435, subclass 4.

Note, new claim 15 is grouped and classified with newly restricted Group II, a method of reducing phosphate re-absorption in a subject comprising delivering a FRP-4 protein. New claims 16-20 are grouped and classified with newly restricted Group III, a method of reducing phosphate re-absorption in a subject comprising delivering a polynucleotide encoding a FRP-4 protein.

Regarding Applicant's arguments that claims 1 to 5 are related in function, that the methods of claims 1 to 5 exhibit a disclosed relationship, and a search of claims 1 to 5 would not represent an undue burden on the Examiner, this is not found persuasive because as argued in the restriction requirement (Paper No. 14), the methods of Groups I and III (claims 1 to 5), while involve similar method steps, use totally different compounds with different chemical properties and structures. Therefore, a search for the compound that alters the activity of a polypeptide encoded by FRP-4 of Group I (claims 1-4) will not encompass all of the art relevant to the FRP-4 protein of Group III (claim 5).

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The IDS and Supplemental IDS, filed 4/29/02 in Paper No. 10 and 1/27/03 in Paper No. 17, respectively, are acknowledged.

Priority

The reference to priority in the first line of the Specification should be updated with current serial numbers where patents have issued. Appropriate correction is required.

Specification

The specification is objected to because the specification at page 7, line 32, recites the terminology "http://www.ncbi.nlm.nih.gov/blast". Embedded hyperlinks and/or other forms of browser-executable code are impermissible and must be deleted. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference. Furthermore, if the application should issue and be placed on the Office web page, the URL may be interpreted as a valid HTML code and become a live web link, transferring an user to a commercial web site. Office policy does not permit the Office to link to any commercial site because the Office exercises no control over the organization, views or accuracy of the information contained on these outside sites. It is noted that page 8, line 6 also contains an embedded hyperlink. The above are examples and are not intended to indicate that the Examiner has made an exhaustive review of

the application. Applicant should remove all embedded hyperlinks for any response to this action to be considered fully responsive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 15 are objected to for reciting the term "FRP-4 protein". The term "FRP-4" should be spelled out in its complete form. Replacement with the language "Frizzled related protein 4 (FRP-4)" would overcome the instant rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim reads on a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein.

The claimed invention encompasses any FRP-4 protein, which includes sequences from any species, mutated sequences, polymorphic and allelic variants, splice variants, sequences that have an unspecified degree of identity (similarity, homology), and so forth. The specification as filed provides only a description of human frizzled-related protein, FRP-4, polynucleotide and amino acid sequences (see SEQ ID NOs. 1 and 2 or Figures 1 and 2, respectively).

The specification provides only a description of human frizzled-related protein, FRP-4, polynucleotide and amino acid sequences. However, the specification as filed, does not provide sufficient description that would allow one of skill in the art to use SEQ ID NOs. 1 and 2 to predict the structures of any FRP-4 protein isolated from other sources, including all polymorphic, allelic and variants of this protein.

The specification fails to describe the complete structure of a representative number of species of the claimed genus. See the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement (Vol. 66, No. 4, pages 1099-1111). These guidelines state that: "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to

show that applicant was in possession of the claimed invention." In the instant case, the specification does not describe or identify characteristics that can be used to distinguish species of the claimed genus.

Additionally, "[T]he skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence."

Applicant's specification does not provide a sufficient number of representative species of FRP-4 protein, which would allow one of skill in the art to predict the structures of all members of the claimed genus of compounds. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Therefore, the specification does not describe the claimed compounds in such full and concise terms so as to indicate that the applicant had possession of these compounds at the time of filing of this application. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.).

Claims 5 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 5 and 15 are drawn to a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein.

The specification as filed provides only a description of human frizzled-related protein, FRP-4, polynucleotide and amino acid sequences (see SEQ ID NOs. 1 and 2 or Figures 1 and 2, respectively).

Schiavi et al. (Current Opinion in Nephrology and Hypertension, 2002 Vol. 11:423-430) assert that, "at present, one can only speculate on the role of FRP gene products in phosphate homeostasis" (see page 426, first paragraph).

Fujita et al. (Journal of Molecular Endocrinology, 2002 Vol. 28:213-223) assert that the biological activities of secreted frizzled proteins remain to be studied, however, they are assumed [emphasis added] to function as modulators of the Wnt-frizzled signaling pathway (see page 219, first column).

Assertions such as those from Schiavi et al. and Fujita et al. indicate that further research is required in the art to understand the function of FRP-4 in phosphate homeostasis and re-absorption.

In view of the unpredictability in the art of the FRp-4 protein, the specification as filed does not provide adequate guidance or examples that would show by correlation how one skilled in the art would practice the claimed invention without having to engage in trial and error or undue experimentation. The specification as filed contemplates a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein. However, the instant

specification does not show any specific link between FRP-4 protein and phosphate re-absorption such that a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein would be an apparent option. It is unclear how the description of the human frizzled-related protein, FRP-4, are correlated with/or representative of a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein. It is also unclear how any FRP-4 protein will reduce phosphate re-absorption in a subject where no specific guidance (i.e. specific mode of treatment, delivery route, tissue specificity, etc.) is provided.

The specification does not provide particular guidance or particular direction for a method of reducing phosphate re-absorption in a subject comprising the FRP-4 protein. The specification does not provide guidance for the delivery of the protein into the target organ and target cells in a subject in quantity sufficient to reduce phosphate re-absorption. While the specification provides a description of human frizzled-related protein, FRP-4, the specification provides no particular nexus between a description of the human frizzled-related protein sequence, FRP-4, and a method of reducing phosphate re-absorption in a subject, as contemplated by the specification. The specification provides no particular guidance of direction for addressing the problems of targeting, permanence and quantity of reducing phosphate re-absorption in a subject, etc, for the FRP-4 protein in a subject. The specification provides no particular guidance or direction for reducing phosphate re-absorption in a subject with FRP-4 protein using any FRP-4 protein of the claimed invention. Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, one of ordinary skill in the art at the time of the invention would have required an

undue amount of experimentation to make and use the claimed invention. Due to the lack of specific guidance in the specification as filed and the lack of correlation between a description of human frizzled-related protein and a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein, one of skill in the art would require specific guidance to practice the current invention. The current specification does not provide such guidance to a method of reducing phosphate re-absorption in a subject comprising delivering the FRP-4 protein and one of skill in the art would be required to perform trial and error or undue experimentation. The quantity of experimentation required to practice the invention would include the de novo determination of how to engineer and deliver a FRP-4 protein such that phosphate re-absorption would be reduced in a subject, particularly, in view of the obstacles needed to overcome to use FRP-4 protein therapy as exemplified in the references discussed above.

Conclusions

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 746-8693 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
March 19, 2003

Ram R. Shukla

RAM R. SHUKLA, PH.D
PATENT EXAMINER